

REMARKS

Reconsideration of this application is respectfully request.

Claims 1, 2 and 9-70 are presently pending in this application. Claims 1, 2, and 9 – 66 are currently rejected. Claims 1, 2, 36, 44, 46, 59, and 61 have been amended. Claims 67 – 70 have been added.

Claims 1, 2, and 36 are amended herein to modify the linkage site. Support for this amendment can be found in the specification. In particular for the linkage through the S¹ site, the reactive >N-R_N or -NR_tR_s or =O group located on Z or W, and other groups that can be first derivatized to a hydroxy or -NR_tR_s group are specifically recited in claim 1. With regard to deletion of S¹, Z or W substituents, and (d) from the claimed linkages to antiviral and/or antineoplastic agents, it is noted that under the rules of practice, if alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. MPEP 2173.05(i) citing *In re Johnson*, 558 F2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977). See also compounds 19, 20, and 22.

Claims 1, 2, 36, 44, 46, 59, and 61 have been amended to delete the zalcitabine from the antiviral agent. Support for this amendment can be found in the claims as originally filed. As noted above, positively recited elements may be explicitly excluded in the claims.

Additional amendments to claims 1, 2, and 36 change only the syntax of the claims.

Support for new claim 67 can be found in the specification at, for example, in Examples 1 – 8. Support for new claim 68 and 69 can be found in claim 1 as originally filed and in paragraph [0087]. New claim 70 is directed to subject matter found in the provisional application 60/390190 (pages 4 and 7 – 11) and is also supported in the present application in claim 1 as originally filed. Support for the terms R^P and OR^P can be found in the provisional application on page 9, last 11 lines and page 10, first 2 lines.

No new matter has been added to the claims.

The Examiner has rejected the claims under 35 U.S.C. §102(a or e) as anticipated, or in the alternative, under 35 U.S.C. §103(a) as obvious over Sympore's 2004/0087517 ('517) and/or US2004/0186063 ('063) publications.

'063 Publication – 35 U.S.C. §102 (a or e) and 35 U.S.C. §103

The '063 publication is a continuation-in-part (CIP) of the '517 publication, also cited herein. It was filed August 20, 2003, after the July 8, 2003 filing date of the present application. Therefore, any information first appearing in the '063 publication not also present in the parent '517 publication cannot be used as prior art to the present application under 35 U.S.C. §102(a) or (e) or §103(a). The '517 publication, which was filed on February 14, 2003, is presumably available as a reference against the present claims under 35 U.S.C. § 102 (e) only. However, this presumption is rebutted.

In the arguments below, we discuss the '517 publication and not the '063 publication. However, all arguments made below in reference to the '517 publication that are similarly available in the '063 publication are herein regarded as made for the '063 publication as well.

'517 Publication – 35 U.S.C. §102(a)

The Examiner has rejected claims 1, 2, and 9 - 66 under 35 U.S.C. §102 (a) as being anticipated by Burnet et al. (US 2004/0087517). The Burnet '517 publication was filed on February 14, 2003 and claims priority to provisional application US 60/357,434, filed Feb. 15, 2002. It was published on May 6, 2004.

This rejection is respectfully traversed. The Burnet '517 publication is not available under 35 U.S.C. §102(a) against any of the pending claims since subject matter disclosed by Burnet was not known or used by others in this country, or described in a printed publication before the invention of claims 1, 2, and 9 - 66. Burnet '517 was published on May 6, 2004 after the filing date of the present nonprovisional application (July 8, 2003), therefore later than the present priority date (July 8, 2002), and there is no indication that the subject matter of Burnet '517 was known or used

in this country before the claimed invention. Accordingly, no claim is anticipated by Burnet under 35 U.S.C. §102(a).

'517 Publication – 35 U.S.C. §102(e)

The Examiner has rejected claims 1, 2, and 9 - 66 under 35 U.S.C. §102 (e) as being anticipated by Burnet et al. (US 2004/0087517).

1. The present invention antedates Burnet

The priority date of the present application is July 8, 2002 based on provisional application 60/359,190. This priority document contains 2 examples and discloses the synthetic route for the preparation of these conjugates. At least one conjugate (compound 1) was made and characterized on or before February 15, 2002, the priority date that the Burnet application asserts, and thus antedates any disclosure in the Burnet nonprovisional application. The pre-February 15, 2002 synthesis and characterization of this compound is supported by the accompanying §1.131 declaration by Linda Tomašković, one of the inventors.

The early synthesis and characterization of this compound demonstrate that the present invention was at least conceived prior to February 15, 2002 (see testimony of and Exhibit A accompanying the Tomašković declaration), and reduced to practice prior to February 15, 2002 (Compound 1, see testimony of and Exhibit B accompanying the Tomašković declaration) and this activity continued and expanded thereafter until the provisional application was filed July 8, 2002. As filed, the provisional application contains 2 examples. The regular application contains 8 examples and describes 22 compounds. This demonstrates that the inventors diligently worked to synthesize and test additional conjugates from prior to February 15, 2002 until the filing of provisional application 60/359,190 and thereafter until the filing date of the present application.

We note that it is not necessary for the applicants to show reduction to practice of the entire scope of the invention. The §131 declaration “must establish possession of either the whole invention claimed or something falling within the claim (such as a species of a claimed genus), in

the sense that the claim as a whole reads on it.” MPEP 715.02 citing *In re Tanczyn*, 347 F.2d 830, 146 USPQ 298 (CCPA 1965).

Compounds of the present invention were understood to have activity at the time of the invention. As provided in the Tomašković declaration and its Exhibit A, the assignee of the present application has had an on-going program addressing anti-inflammatory conjugates since before February 15, 2002. Conjugates having an “anti-inflammatory subunit that can be steroid or nonsteroid” (Declaration Exhibit A pg 4: 2-3) were developed by the assignee no later than January 3, 2002 for their anti-inflammatory activity. Therefore, the utility of compound such as those described in the present invention was contemplated prior to February 15, 2002.

Therefore, since the present invention was both conceived and reduced to practice prior to the filing date of either of the Burnet provisional or non provisional patent application, the rejection under 35 U.S.C. §102(e) based on the Burnet application has been overcome and its withdrawal is respectfully requested.

2. Burnet Provisional fails to disclose the claimed compounds.

Even if the Burnet non provisional (“517) application had been available as a reference under 35 U.S.C. §102(e), it would still not anticipate the present compounds.

The ‘517 publication and provisional application do not provide sufficient teachings to describe the conjugates of claims 1, 2, and 9 – 66. According to the Burnet provisional application, a “transportophore” can encompass a variety of molecules, including broad classes of compounds such as alcohols and organic acids. Specifically, transportophores are described in the provisional Burnet specification at page 3 line 23 to page 4 line 2 as follows:

The transportophore can be a metabolite (such as an amino acid or peptide), a natural product, a metabolite derivative (e.g., a sugar, amino, or peptide derivative), an organic acid an organic base, a nucleobase, or an alcohol. It can be an amphiphilic molecule having a pKa value of 6.5 to 9.5, or a cyclic or heterocyclic molecule (e.g.,

lactone, lactam, ether, cyclic acetal, or hemi-acetal). The cyclic or heterocyclic molecule can have an attached sugar. The cyclic or heterocyclic molecule can be a macrolactone or macroether, including a macrolactone or macroether having an attached sugar. The cyclic or heterocyclic molecule can also be a macrolide or ketolide having an amino sugar, including a macrolide having mono-, di-, or tri-basic groups (e.g., an amine).

The largely functional characterizations above encompass countless molecules. For instance, although a “metabolite derivative” is exemplified in Burnet as “a sugar, amino, or peptide derivative,” this language does little to narrow the scope of compounds included in its definition because “amino,” for example, includes any compound having an -NH₂ group. The other types of listed transportophores are at least as broad as metabolite derivatives. A “natural product,” for example, is seemingly limitless and could comprise any compound that is not synthetic. The term “alcohol” is similarly wide-ranging and includes any alkyl compound containing a hydroxyl group. Likewise, an “organic acid” includes a vast number of compounds that contain carboxyl group(s). A similar comment can be made about the extensive breadth of the other types of transportophores quoted above as well.

Additionally, the term, “therapeutic agent,” introduced in the Burnet provisional at page 31, lines 12-22, as follows:

A “therapeutic agent,” as used herein, is a molecule with pharmacological activity (e.g., a therapeutic agent, medicine, medicament, or active agent), a disease modification agent, or any other molecule that can be covalently attached to a transportophore via a bond or a linker which may have a desirable mode of action in immune cells.

The term “therapeutic agent” includes a myriad of compounds without limitation as to structure or pharmacological activity, or mechanism for exerting such activity. The provisional specification provides a long, yet “non-exclusive,” list of classes of therapeutic agents on page 36

line 26 to page 40 line 16. Yet, these examples illustrate only a small number of therapeutic agents that could be coupled to an even smaller number of illustrated transportophores. For the reasons advanced above regarding the transportophore, this scanty description of therapeutic agents and scanty pairing of such agents with transportophores, is insufficient to circumscribe for a person of ordinary skill the group of conjugates included claims 1, 2, and 9 – 66 of the present invention. There is simply no guidance, except:

the provisional application's 15 specific macrolide-NSAID conjugates and 8 NSAID conjugates in Burnet '517,

the 4 specific macrolide-steroids conjugates in Burnet '517 (linked through the C/2' or C/3' on the desosamine sugar (S1)),

the 2 macrolide-antineoplastic agent conjugates provided in the provisional application (linked through the C/2' position on the desosamine sugar (S1)), and

the provisional application's 8 macrolide-antiviral agent and 5 macrolide-antiviral conjugates in Burnet '517 linked through the C/2' or C/3' on the desosamine sugar (S1) or C/9 position of the macrolide.

There is no further information as to which transportophores can be paired with which therapeutic agents, not to mention at which point on the molecule the former should be linked to the latter without destroying either the targeting ability of the transportophore or the therapeutic activity of the therapeutic agent. Although a reference may be relied upon for all that it would have reasonably suggested to one of ordinary skill in the art (MPEP 2123 citing *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert denied 493 U.S. 975 (1989)), the vague broad and unfocused disclosure regarding the non-antibiotic therapeutic agent only exacerbates the insufficiency of the disclosure identified with respect to the transportophore.

In our view, the examples with their illustration of only a narrow group of transportophores conjugated with the particular therapeutic agents do not provide support for the

particular macrolides and active subunit of the claimed invention. The disclosure does not place a person of ordinary skill in possession of the subgenus of conjugates, in which the transportophore is suited to the non-antibiotic therapeutic agent, the point of linkage does not destroy function in one or the other.

The Burnet provisional application, in examples 2 – 35, contains 56 macrolide transportophore conjugates. There is no indication about what type of therapeutic agent can be conjugated to these macrolides other than the particular therapeutic agents described.

Lastly, the Burnet specification does not disclose the point of attachment between the linker and the transportophore and between the linker and the non-antibiotic therapeutic agent, other than by generally stating that the linker attaches through its “functional group”— a term that is nearly limitless in scope. Nor does the Burnet specification indicate where the point of attachment should be between the therapeutic agent and the transportophore in those conjugates that contain a bond in place of a linker.

Of the 56 macrolide conjugates exemplified in the Burnet provisional application, 33 of them contain a therapeutic agent attached through the desosamine C-2' or C-3' sugar on a macrolide transportophore; 22 contain a therapeutic agent attached at the C/9 or N/9a position on a macrolide ring; and one contains a therapeutic agent attached through a pendent oxygen atom (C/3) of a macrolide ring.

In our view, the Burnet disclosure of only narrow groups of conjugates (out of the numerous possibilities encompassed by the scope of possible conjugates), and of a limited number of modes and sites of attachment of the transportophore to the therapeutic agent, does not provide sufficient teachings to anticipate the claims of the present invention.

The currently pending claims limit the linker L to a peptide when V is a steroid or NSAID. For these conjugates as well as antineoplastic or antiviral agents linked via a peptide, the ‘517 publication does not anticipate the claimed invention since it does not disclose any compounds having a peptide linker. The ‘517 publication broadly discloses that the linker is “typically a

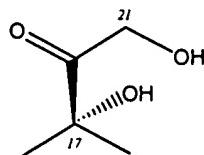
bifunctional molecule of low molecular mass,” (para. 515) but then states that “[l]inkers have the following formula: $F^1—M—F^2$ where the definition of M, F^1 and F^2 do not encompass peptides within the linker formula (para 516). All linkers described in the ‘517 publication contain this linker moiety and therefore do not suggest the use of peptides as linkers. Similarly, the linkers described in the provisional application (see pg 28, last line to pg 30) also are described by the formula $F^1—M—F^2$. This generic terminology does not teach the use of the peptides as claimed in the present invention.

Therefore, for claims 1, 2, and 9 – 66, when L is a peptide are not anticipated by the claimed invention. Similarly, claims 69 – 70 are not anticipated by the Burnet ‘517 publication since these claims are limited to peptide linkers.

Conjugates where V is (i) an anti-inflammatory steroid subunit:

In particular for steroid conjugates, the ‘517 publication contains four steroid-macrolide conjugates, none having a peptide linker. Further, there are no steroid conjugates included in the provisional application on which the ‘517 publication is based.

Additionally, each of the steroid conjugates disclosed in the ‘517 publication (compounds 82, 83, 85 and 86) do not teach the conjugates presently claimed for at least the reason that the steroid component is different from the steroids in the present claims. Even though Burnet lists corticosteroids as a general class of therapeutic agents, there is no specific teaching in Burnet ‘517 that a corticosteroid can be modified to remove the C21 carbon and terminal OH found on the corticosteroid.



Therefore, none of the steroid-macrolide conjugates of the present claims are anticipated by the ‘517 publication.

Conjugates where V is (ii) a non-steroidal anti-inflammatory subunit:

Although several of the known NSAIDs exemplified in conjugates in the presently claimed invention are disclosed as conjugated therapeutic agents in the '517 publication, none of these NSAIDS are linked via a peptide linker. Therefore, none of the NSAID-macrolide conjugates of the present claims are anticipated by the '517 publication. Therefore, there is no anticipation of claims 1, 2, or 9 – 70 wherein V is an NSAID subunit

Conjugates where V is (iii) an antineoplastic subunit:

The '517 publication discloses a melphalan conjugate (compound 186) and a chlorambucil conjugate (compound 144); both of the conjugates are linked to a macrolide through the desosamine C2' position, which is located on the S₁ sugar as described by the formula in presently pending claim 1. The related Burnet provisional lists melphalan in a table of therapeutic agents (pg 49, line 31) that can be used as a conjugated moiety, but no example is directed to such a conjugate and no discussion of the linkage site for such a conjugate is provided.

The claims of the present invention are currently limited to conjugates and their use wherein if V is an antineoplastic subunit, the linkage site is not on the S¹ sugar. Therefore, there is no anticipation of claims 1, 2, or 9 – 70 wherein V is an antineoplastic subunit.

Conjugates where V is (iv) an antiviral subunit:

The '517 publication discloses a ribavirin conjugate (compound 97), an abacavir conjugate (compound 90), zidovudine conjugates (compounds 92, 94, and 101), and describes a number of alcohols that can be conjugated in Table 3. The provisional application of '517 provides additional conjugates including ribavirin (compound 122), famciclovir (compound 117), lamivudine (compound 118), and amprenavir (compound 125). Each of these conjugates are linked to the macrolide through the desosamine C/2' or C/3' position on the S¹ sugar or through the macrolide C/9 position. The provisional application additionally lists zalcitabine conjugates (compounds 128-

131); however, antiviral agents containing zalcitabine are not within the scope of the currently claimed invention.

The claims of the present invention are currently limited to conjugates and their use wherein if V is an antiviral subunit, the linkage site is not on the S¹ sugar or at C/9. Therefore, there is no anticipation of claims 1, 2, or 9 – 70 wherein V is an antiviral subunit.

3. None of claims 1 – 70 are anticipated by Burnet

Claim 1

Accordingly, Burnet does not anticipate claim 1 under 35 U.S.C. § 102(e) at least because the reference is removed by the showing of prior invention as discussed above.

The attached declarations by Linda Tomašković and Višnja Poljak, show that a conception and diligent reduction to practice of the present invention occurred prior to the filing of the Burnet provisional application. Exhibit B for the Tomašković declaration includes the pages of the laboratory notebooks recording the synthesis and characterization (by mass spectrometry and yield) of a compound made prior to February 15, 2002. This compound, also identified in claim 14, is within the scope of claim 1. This evidence demonstrates that the Inventors had conceived and reduced the invention to practice before the Burnet provisional application was filed. Further, the scope of the provisional patent application as filed show further that the Inventors diligently worked on this invention, as Declarant Tomašković testifies, from conception to reduction to practice the latter including actual reduction to practice and to the filing of the provisional application. Exhibit A for the Poljak declaration includes the pages of the laboratory notebooks recording the synthesis and characterization (by mass spectrometry and yield) of a compound made prior to February 14, 2003. This compound, also identified in claim 15, is within the scope of claim 1. Therefore, since the Burnet application was not filed before the present invention was conceived and reduced to practice, it is not available as a reference under 35 U.S.C. §102(e).

In addition, Claim 1 of the present invention has been limited to compositions wherein if V is an antineoplastic subunit or an antiviral subunit, the linkage site is not on S¹ and compositions wherein if V is an antiviral subunit, Z or W is :>C=O or >N-R_N.

Anticipation requires that each and every element of the rejected claim be disclosed in a single prior art reference. See, M.P.E.P. § 2131. Every element of the claimed invention must be literally present, arranged as in the claim. *Perkin Elmer Corp. v. Computervision Corp.*, 732 F.2d 888, 894, 221 USPQ 669, 673 (Fed. Cir. 1984). A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Since each element of claim 1 is not disclosed in Burnet '517 or in the Burnet priority document, this claim would not be anticipated, even if the Burnet documents were available as references.

Claims 2, 9 – 13, and 52

Since claim 1 is not anticipated, it follows that claim 2, dependent on claim 1 and claims 9 – 13 and 52, dependent on claim 2, are similarly not anticipated.

Claims 14 - 35

None of the compounds in these claims are disclosed by Burnet. Therefore, rejection under 35 U.S.C. §102 is improper. Applicants respectfully ask for this rejection to be withdrawn.

Claim 36

Since Burnet does not anticipate the product claim as discussed above, the subject matter of claim 36, a process for making the novel conjugates of claim 1, is also not anticipated.

In addition, the processes of claim 36 are not taught by Burnet. Burnet discloses mixing the therapeutic agent with linkers (e.g., succinic anhydride, glutaric acid, or carbonyldiimidazole)

and then combining the transportophore (e.g., macrolide); this does not anticipate the present process.

Claims 37

Burnet does not anticipate the pharmaceutical composition of claim 37 since the claimed pharmaceutical compositions are limited to compounds of claim 1, which are not anticipated as shown above, and to derivatives of such compounds, which are also not anticipated by Burnet.

Claims 38 - 51 and 53 – 66

These claims are drawn to methods of using the product of claim 1 or a claim dependent on claim 1 and are not anticipated by Burnet at least for the reason that the product of claim 1 is not anticipated by Burnet.

Therefore, applicants respectfully request that the rejection under 35 U.S.C. §102 be withdrawn for claims 1, 2, and 9 – 66.

New claims 67 – 70

New claims 67 – 68 are similarly not anticipated by the Burnet ‘517 publication since claims 67 – 68 are dependent on claim 1 and claim 1 is not anticipated.

Claim 69, which is limited to conjugates having a peptide linker molecule, is similarly not anticipated by Burnet ‘517 under 35 U.S.C. § 102(e), not only because it has been removed as a reference under 35 U.S.C. § 102(e) by the present showing of prior invention but also—and independently—because Burnet ‘517 does not disclose peptide linkers. In order to anticipate, each and every element of the claim must be disclosed. Therefore, this claim is not anticipated.

Claim 70 is similarly not anticipated by Burnet ‘517 under 35 U.S.C. § 102(e) since Burnet ‘517 has been removed as a reference, as stated above. The subject matter of Claim 70 was identically present in the provisional application filed July 8, 2002, (from which the present

application claims priority). This filing date is prior to the filing date of Burnet '517. The Burnet provisional application has a filing date of February 15, 2002. However, as stated above, the general teaching of the Burnet provisional application is insufficient to anticipate compounds of claim 70.

'517 Publication – 35 U.S.C. §103

The Examiner has rejected claims 1, 2, and 9 – 66 under 35 U.S.C. §103(a) as being unpatentable over Burnet et al. (US 2004/0087517), stating that a person of ordinary skill in the art would have found any differences to be minor in nature, and the invention would have been *prima facie* obvious.

The rejection is respectfully traversed, and reconsideration is requested. Therefore Applicants respectfully request reconsideration and withdrawal of this rejection.

The Burnet '517 document has been overcome as a reference under 35 U.S.C. § 102 by the present showing of prior invention. Therefore, it is similarly not available under 35 U.S.C. § 103. Therefore, the rejection is respectfully traversed, and reconsideration is requested. Additionally, as will be shown below, the teaching of Burnet is inadequate to disclose or suggest the present compounds. Burnet would not have been used to show that a person of ordinary skill in the art would have been motivated to link a steroid, NSAID, antiviral agent, or antineoplastic agent and 14- and 15-membered macrolide subunits to form the conjugates of the presently claimed invention.

In addition, the scope of the compounds, compositions, and methods covered by claims 1, 2, and 9 – 70 are not made obvious by Burnet since Burnet teaches away from modifying the compounds he discloses to obtain any other compounds including closely related compounds. Burnet states “similar molecules with similar properties can exhibit quite different uptake into immune cells, hence the difficulty in employing general specifications known in the art” (para. 0728), teaching away from departures from the structure of specific compounds disclosed therein. Burnet does not teach any locations that are useful for linking the macrolide conjugate to therapeutic agents other than the ones particularly disclosed in the examples. Burnet also does not teach what

modifications can be made on the substituents on the macrolide ring in order to obtain a useful compound. Instead, Burnet indicates that an “empirical method is the only reliable means of selecting and guiding synthetic chemistry” towards the conjugate compounds (para. 0729). This is insufficient to constitute a suggestion of any of the compounds claimed in the present application, and instead constitutes a negative teaching, a so-called “teach away.”

Applicants submit that the presently claimed conjugates are not *prima facie* obvious over the teaching of Burnet. It is not obvious to conjugate the particular circumscribed class of macrolides as claimed to the claimed steroid, NSAID, antiviral agent, or antineoplastic agent based on the teachings of Burnet since Burnet teaches that similar molecules can exhibit quite different uptake into immune cells (para. 0728). The conjugates containing the peptide linkers of the present claims are not obvious in view of the linkers disclosed in the ‘517 publication. These linkers are structurally dissimilar, and additionally form part of particularly disclosed embodiments of the present invention, particularly where NSAIDS and steroids are used as the subunit V (see the application, para. 0090-0092).

Burnet ‘517 does not disclose any macrolide-steroid conjugates other than the four conjugates in the non-provisional application, does not teach how to obtain the macrolide-steroid conjugates as claimed in the present invention that would display significant uptake into immune cells, and does not disclose any macrolide-steroid conjugates linked via a peptide linker. Therefore, for ease of the applicable foregoing reasons, the present steroid conjugates are not obvious.

Similarly, Burnet ‘517 does not disclose any macrolide-NSAID conjugates other than 15 conjugates in the provisional application and the 8 additional compounds in the published application, does not teach how to obtain the macrolide-NSAID conjugates claimed in the present invention that display significant uptake into immune cells, and does not disclose any macrolide-NSAID conjugates linked via a peptide linker as claimed in the present invention. Therefore, the present NSAID conjugates are not obvious.

Additionally, Burnet '517 does not disclose macrolide-antineoplastic conjugates except for the two conjugates provided in the non-provisional application or any macrolide-antiviral agents other than the 5 conjugates in the non-provisional application and 8 conjugates in the provisional application.

Therefore, the present claims are not obvious in view of Burnet '517. Accordingly, in view of the amendments and arguments set forth above, it is submitted that the claimed subject matter would not have been obvious to one of ordinary skill in the art over Burnet '517. Applicants respectfully request that the rejections be withdrawn.

As explained above, Burnet '063 was filed after the filing date of the present application and is not available as a reference against the present claims except to the extent that it can rely on the original disclosure of the '517 application. However, as we demonstrated above, the '517 application fails to anticipate the present claims or make the present claims obvious, hence the '063 application cannot do so either.

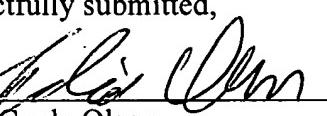
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Accordingly, the pending claims in this application are believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to enter this Amendment, and to pass this application to issue.

Therefore, applicants respectfully request that this rejection for claims 1, 2, and 9 - 66 be withdrawn. Since, the present amendment places the application in condition for allowance and does not require further consideration and/or searching by the Examiner, the present amendment should be entered.

Dated: May 26, 2006

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